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## NOTICE OF ALLOWANCE AND FEE(S) DUE

28986 7590 08/10/2010

HARRIET M. STRIMPEL, D. Phil.  
New England Biolabs, Inc.  
240 COUNTY ROAD  
IPSWICH, MA 01938-2723

EXAMINER

RAMIREZ, DELIA M

ART UNIT

PAPER NUMBER

1652

DATE MAILED: 08/10/2010

APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
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10/585,964

07/13/2006

Chudi Guan

NEB-236-PUS

7911

TITLE OF INVENTION: MODIFIED DNA CLEAVAGE ENZYMES AND METHODS FOR USE (AS AMENDED BY ISA)

APPLN. TYPE	SMALL ENTITY	ISSUE FEE DUE	PUBLICATION FEE DUE	PREV. PAID ISSUE FEE	TOTAL FEE(S) DUE	DATE DUE
nonprovisional	YES	\$755	\$300	\$0	\$1055	11/10/2010

**THE APPLICATION IDENTIFIED ABOVE HAS BEEN EXAMINED AND IS ALLOWED FOR ISSUANCE AS A PATENT. PROSECUTION ON THE MERITS IS CLOSED. THIS NOTICE OF ALLOWANCE IS NOT A GRANT OF PATENT RIGHTS. THIS APPLICATION IS SUBJECT TO WITHDRAWAL FROM ISSUE AT THE INITIATIVE OF THE OFFICE OR UPON PETITION BY THE APPLICANT. SEE 37 CFR 1.313 AND MPEP 1308.**

**THE ISSUE FEE AND PUBLICATION FEE (IF REQUIRED) MUST BE PAID WITHIN THREE MONTHS FROM THE MAILING DATE OF THIS NOTICE OR THIS APPLICATION SHALL BE REGARDED AS ABANDONED. THIS STATUTORY PERIOD CANNOT BE EXTENDED. SEE 35 U.S.C. 151. THE ISSUE FEE DUE INDICATED ABOVE DOES NOT REFLECT A CREDIT FOR ANY PREVIOUSLY PAID ISSUE FEE IN THIS APPLICATION. IF AN ISSUE FEE HAS PREVIOUSLY BEEN PAID IN THIS APPLICATION (AS SHOWN ABOVE), THE RETURN OF PART B OF THIS FORM WILL BE CONSIDERED A REQUEST TO REAPPLY THE PREVIOUSLY PAID ISSUE FEE TOWARD THE ISSUE FEE NOW DUE.**

### HOW TO REPLY TO THIS NOTICE:

#### I. Review the SMALL ENTITY status shown above.

If the SMALL ENTITY is shown as YES, verify your current SMALL ENTITY status:

A. If the status is the same, pay the TOTAL FEE(S) DUE shown above.

B. If the status above is to be removed, check box 5b on Part B - Fee(s) Transmittal and pay the PUBLICATION FEE (if required) and twice the amount of the ISSUE FEE shown above, or

If the SMALL ENTITY is shown as NO:

A. Pay TOTAL FEE(S) DUE shown above, or

B. If applicant claimed SMALL ENTITY status before, or is now claiming SMALL ENTITY status, check box 5a on Part B - Fee(s) Transmittal and pay the PUBLICATION FEE (if required) and 1/2 the ISSUE FEE shown above.

II. PART B - FEE(S) TRANSMITTAL, or its equivalent, must be completed and returned to the United States Patent and Trademark Office (USPTO) with your ISSUE FEE and PUBLICATION FEE (if required). If you are charging the fee(s) to your deposit account, section "4b" of Part B - Fee(s) Transmittal should be completed and an extra copy of the form should be submitted. If an equivalent of Part B is filed, a request to reapply a previously paid issue fee must be clearly made, and delays in processing may occur due to the difficulty in recognizing the paper as an equivalent of Part B.

III. All communications regarding this application must give the application number. Please direct all communications prior to issuance to Mail Stop ISSUE FEE unless advised to the contrary.

**IMPORTANT REMINDER: Utility patents issuing on applications filed on or after Dec. 12, 1980 may require payment of maintenance fees. It is patentee's responsibility to ensure timely payment of maintenance fees when due.**

# **PART B - FEE(S) TRANSMITTAL**

**Complete and send this form, together with applicable fee(s), to: Mail Mail Stop ISSUE FEE  
Commissioner for Patents  
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Alexandria, Virginia 22313-1450  
or Fax (571)-273-2885**

INSTRUCTIONS: This form should be used for transmitting the ISSUE FEE and PUBLICATION FEE (if required). Blocks 1 through 5 should be completed where appropriate. All further correspondence including the Patent, advance orders and notification of maintenance fees will be mailed to the current correspondence address as indicated unless corrected below or directed otherwise in Block 1, by (a) specifying a new correspondence address; and/or (b) indicating a separate "FEE ADDRESS" for maintenance fee notifications.

CURRENT CORRESPONDENCE ADDRESS (Note: Use Block 1 for any change of address)

28986 7590 08/10/2010

**HARRIET M. STRIMPEL, D. Phil.**  
New England Biolabs, Inc.  
240 COUNTY ROAD  
IPSWICH, MA 01938-2723

Note: A certificate of mailing can only be used for domestic mailings of the Fee(s) Transmittal. This certificate cannot be used for any other accompanying papers. Each additional paper, such as an assignment or formal drawing, must have its own certificate of mailing or transmission.

## **Certificate of Mailing or Transmission**

I hereby certify that this Fee(s) Transmittal is being deposited with the United States Postal Service with sufficient postage for first class mail in an envelope addressed to the Mail Stop ISSUE FEE address above, or being facsimile transmitted to the USPTO (571) 273-2885, on the date indicated below.

(Depositor's name)
(Signature)
(Date)

APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
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10/585,964 07/13/2006 Chudi Guan NEB-236-PUS 7911

TITLE OF INVENTION: MODIFIED DNA CLEAVAGE ENZYMES AND METHODS FOR USE (AS AMENDED BY ISA)

APPLN. TYPE	SMALL ENTITY	ISSUE FEE DUE	PUBLICATION FEE DUE	PREV. PAID ISSUE FEE	TOTAL FEE(S) DUE	DATE DUE
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nonprovisional YES \$755 \$300 \$0 \$1055 11/10/2010

EXAMINER	ART UNIT	CLASS-SUBCLASS
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RAMIREZ, DELIA M 1652 435-199000

1. Change of correspondence address or indication of "Fee Address" (37 CFR 1.363).

- ☐ Change of correspondence address (or Change of Correspondence Address form PTO/SB/122) attached.
- ☐ "Fee Address" indication (or "Fee Address" Indication form PTO/SB/47; Rev 03-02 or more recent) attached. **Use of a Customer Number is required.**

2. For printing on the patent front page, list

- (1) the names of up to 3 registered patent attorneys or agents OR, alternatively, 1 \_\_\_\_\_
- (2) the name of a single firm (having as a member a registered attorney or agent) and the names of up to 2 registered patent attorneys or agents. If no name is listed, no name will be printed. 2 \_\_\_\_\_
- 3 \_\_\_\_\_

3. ASSIGNEE NAME AND RESIDENCE DATA TO BE PRINTED ON THE PATENT (print or type)

PLEASE NOTE: Unless an assignee is identified below, no assignee data will appear on the patent. If an assignee is identified below, the document has been filed for recordation as set forth in 37 CFR 3.11. Completion of this form is NOT a substitute for filing an assignment.

(A) NAME OF ASSIGNEE (B) RESIDENCE: (CITY and STATE OR COUNTRY)

Please check the appropriate assignee category or categories (will not be printed on the patent) : ☐ Individual ☐ Corporation or other private group entity ☐ Government

4a. The following fee(s) are submitted:

- ☐ Issue Fee
- ☐ Publication Fee (No small entity discount permitted)
- ☐ Advance Order - # of Copies \_\_\_\_\_

4b. Payment of Fee(s); (Please first reapply any previously paid issue fee shown above)

- ☐ A check is enclosed.
- ☐ Payment by credit card. Form PTO-2038 is attached.
- ☐ The Director is hereby authorized to charge the required fee(s), any deficiency, or credit any overpayment, to Deposit Account Number \_\_\_\_\_ (enclose an extra copy of this form).

5. Change in Entity Status (from status indicated above)

- ☐ a. Applicant claims SMALL ENTITY status. See 37 CFR 1.27. ☐ b. Applicant is no longer claiming SMALL ENTITY status. See 37 CFR 1.27(g)(2).

NOTE: The Issue Fee and Publication Fee (if required) will not be accepted from anyone other than the applicant; a registered attorney or agent; or the assignee or other party in interest as shown by the records of the United States Patent and Trademark Office.

Authorized Signature \_\_\_\_\_

Date \_\_\_\_\_

Typed or printed name \_\_\_\_\_

Registration No. \_\_\_\_\_

This collection of information is required by 37 CFR 1.311. The information is required to obtain or retain a benefit by the public which is to file (and by the USPTO to process) an application. Confidentiality is governed by 35 U.S.C. 122 and 37 CFR 1.14. This collection is estimated to take 12 minutes to complete, including gathering, preparing, and submitting the completed application form to the USPTO. Time will vary depending upon the individual case. Any comments on the amount of time you require to complete this form and/or suggestions for reducing this burden, should be sent to the Chief Information Officer, U.S. Patent and Trademark Office, U.S. Department of Commerce, P.O. Box 1450, Alexandria, Virginia 22313-1450. DO NOT SEND FEES OR COMPLETED FORMS TO THIS ADDRESS. SEND TO: Commissioner for Patents, P.O. Box 1450, Alexandria, Virginia 22313-1450.

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10/585,964	07/13/2006	Chudi Guan	NEB-236-PUS	7911
28986	7590	08/10/2010	EXAMINER	
HARRIET M. STRIMPEL, D. Phil. New England Biolabs, Inc. 240 COUNTY ROAD IPSWICH, MA 01938-2723			RAMIREZ, DELIA M	
			ART UNIT	PAPER NUMBER
			1652	
DATE MAILED: 08/10/2010				

## Determination of Patent Term Adjustment under 35 U.S.C. 154 (b) (application filed on or after May 29, 2000)

The Patent Term Adjustment to date is 282 day(s). If the issue fee is paid on the date that is three months after the mailing date of this notice and the patent issues on the Tuesday before the date that is 28 weeks (six and a half months) after the mailing date of this notice, the Patent Term Adjustment will be 282 day(s).

If a Continued Prosecution Application (CPA) was filed in the above-identified application, the filing date that determines Patent Term Adjustment is the filing date of the most recent CPA.

Applicant will be able to obtain more detailed information by accessing the Patent Application Information Retrieval (PAIR) WEB site (<http://pair.uspto.gov>).

Any questions regarding the Patent Term Extension or Adjustment determination should be directed to the Office of Patent Legal Administration at (571)-272-7702. Questions relating to issue and publication fee payments should be directed to the Customer Service Center of the Office of Patent Publication at 1-(888)-786-0101 or (571)-272-4200.

<b>Notice of Allowability</b>	<b>Application No.</b>	<b>Applicant(s)</b>	
	10/585,964	GUAN ET AL.	
	<b>Examiner</b>	<b>Art Unit</b>	
	DELIA M. RAMIREZ	1652	

**-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address--**

All claims being allowable, PROSECUTION ON THE MERITS IS (OR REMAINS) CLOSED in this application. If not included herewith (or previously mailed), a Notice of Allowance (PTOL-85) or other appropriate communication will be mailed in due course. **THIS NOTICE OF ALLOWABILITY IS NOT A GRANT OF PATENT RIGHTS.** This application is subject to withdrawal from issue at the initiative of the Office or upon petition by the applicant. See 37 CFR 1.313 and MPEP 1308.

1. ☒ This communication is responsive to 7/27/2010.
2. ☒ The allowed claim(s) is/are 29,30,32,36-39 and 41-44.
3. ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All    b) ☐ Some\*    c) ☐ None    of the:
1. ☐ Certified copies of the priority documents have been received.
2. ☐ Certified copies of the priority documents have been received in Application No. \_\_\_\_.
3. ☐ Copies of the certified copies of the priority documents have been received in this national stage application from the International Bureau (PCT Rule 17.2(a)).
- \* Certified copies not received: \_\_\_\_.

Applicant has THREE MONTHS FROM THE "MAILING DATE" of this communication to file a reply complying with the requirements noted below. Failure to timely comply will result in ABANDONMENT of this application.

**THIS THREE-MONTH PERIOD IS NOT EXTENDABLE.**

4. ☐ A SUBSTITUTE OATH OR DECLARATION must be submitted. Note the attached EXAMINER'S AMENDMENT or NOTICE OF INFORMAL PATENT APPLICATION (PTO-152) which gives reason(s) why the oath or declaration is deficient.
5. ☐ CORRECTED DRAWINGS ( as "replacement sheets") must be submitted.
- (a) ☐ including changes required by the Notice of Draftsperson's Patent Drawing Review ( PTO-948) attached
- 1) ☐ hereto or 2) ☐ to Paper No./Mail Date \_\_\_\_.
- (b) ☐ including changes required by the attached Examiner's Amendment / Comment or in the Office action of Paper No./Mail Date \_\_\_\_.
- Identifying indicia such as the application number (see 37 CFR 1.84(c)) should be written on the drawings in the front (not the back) of each sheet. Replacement sheet(s) should be labeled as such in the header according to 37 CFR 1.121(d).**
6. ☐ DEPOSIT OF and/or INFORMATION about the deposit of BIOLOGICAL MATERIAL must be submitted. Note the attached Examiner's comment regarding REQUIREMENT FOR THE DEPOSIT OF BIOLOGICAL MATERIAL.

**Attachment(s)**

- |   |  |
|---|--|
| <p>1. <input type="checkbox"/> Notice of References Cited (PTO-892)</p> <p>2. <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948)</p> <p>3. <input type="checkbox"/> Information Disclosure Statements (PTO/SB/08),<br/>Paper No./Mail Date ____</p> <p>4. <input type="checkbox"/> Examiner's Comment Regarding Requirement for Deposit of Biological Material</p> | <p>5. <input type="checkbox"/> Notice of Informal Patent Application</p> <p>6. <input type="checkbox"/> Interview Summary (PTO-413),<br/>Paper No./Mail Date ____.</p> <p>7. <input checked="" type="checkbox"/> Examiner's Amendment/Comment</p> <p>8. <input checked="" type="checkbox"/> Examiner's Statement of Reasons for Allowance</p> <p>9. <input type="checkbox"/> Other ____.</p> |
|---|--|

## **DETAILED ACTION**

### ***Status of the Application***

Claims 18-23, 25, 29-30, 32, 36-39, 41-47 are pending.

Amendment of claims 32, 36-39, 41-44 and cancellation of claims 33-34, 40 as submitted in a communication filed on 7/27/2010 are acknowledged.

In a telephone conversation with Ms Harriet Strimpel on 8/3/2010, an agreement was reached to amend claims 29-30, 36, 38, 42-44 and cancel claims 18-23, 25, 45-47 to place the application in condition for allowance.

In accordance with MPEP 821.04, claims 29-30 are rejoined for examination on the merits in view of the fact that the product claims have been found allowable. The previous restriction between the elected product and the methods of claims 29-30 (Groups IV and V) is hereby withdrawn.

### ***Examiner's Amendment***

1. An extension of time under 37 CFR 1.136(a) is required in order to make an examiner's amendment which places this application in condition for allowance. In the response filed on 7/27/2010 (Conclusion section), Ms Harriet Strimpel requested an extension of time and authorized the Director to charge Deposit Account No. 14-0740 in the amount of \$ 825.00. Ms Strimpel also authorized charging any deficiencies to the same account as stated in the response of 7/27/2010.
2. Authorization for this Examiner's amendment was given in a telephone interview with Ms Harriet Strimpel on 8/3/2010. Should the changes and/or additions be unacceptable to applicant, an amendment may be filed as provided by 37 CFR 1.312. To ensure consideration of such an amendment, it MUST be submitted no later than the payment of the issue fee.
3. Please cancel claims 18-23, 25, 45-47.
4. Please replace claims 29-30, 36, 38, 42-44 as follows:

29. A method of forming a shotgun cloning library, comprising:
- (a) incubating the composition of claim 32 with a DNA to form non-sequence specific cleavage fragments of the DNA that are ligatable; the ligatable DNA being capable of insertion into a vector for cloning into a vector for cloning in a host cell; and
  - (b) forming the shotgun cloning library.
30. A method for mapping nicks in a duplex DNA, comprising:
- (a) incubating the composition of claim 32 with the duplex DNA in a manganese-containing buffer;
  - (b) permitting nicking to occur across from a pre-existing nick site to form fragments of the duplex DNA with single strand overhangs; and
  - (c) mapping the nicks in the DNA.
36. The composition according to claim 32, wherein the endonuclease activity comprises greater DNA cleavage activity of the variant T7 Endo I polypeptide in a manganese-containing buffer compared with the DNA cleavage activity of the parent T7 Endo I polypeptide in the manganese-containing buffer.
38. The composition according to claim 32, wherein the endonuclease activity comprises reduced DNA cleavage activity of the variant T7 Endo I polypeptide in a magnesium-containing buffer compared with the DNA cleavage activity of the parent T7 Endo I polypeptide in the magnesium-containing buffer.

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42. The composition according to claim 41, wherein the substitution is a single amino acid substitution, a dipeptide substitution, a tripeptide substitution, or a tetrapeptide substitution; or wherein the deletion is a deletion of the PA dipeptide, deletion of Pro, or deletion of Ala.

43. The composition according to claim 42, wherein the PA dipeptide is substituted with an Ala (A), a Lys (K), a Gly (G), an Asp (D), a Pro (P), an Ala-Ala (AA) dipeptide, an Ala-Gly-Ala (AGA) tripeptide, or a Pro-Ala-Pro-Ala (PAPA) peptide.

44. A kit comprising the composition of claim 41.

#### ***Reasons for Allowance***

5. The following is an Examiner's statement of reasons for allowance. Although the prior art discloses variants of the T7 Endo I nuclease, the Examiner has found no teaching or suggestion in the prior art directed to variants of the T7 Endo I nuclease which differ from the wild-type T7 Endo I nuclease only by changes within positions corresponding to positions 44-49 of the polypeptide of SEQ ID NO: 12. Therefore, claims 29-30, 32, 36-39, 41-44, directed to a composition comprising a variant of the T7 Endo I nuclease which differs from the wild-type T7 Endo I nuclease only by changes within positions corresponding to positions 44-49 of the polypeptide of SEQ ID NO: 12, a kit comprising said composition, a method of forming a shotgun cloning library using said composition, and a method for mapping nicks in a duplex DNA using such composition, are allowable over the prior art of record.

#### ***Conclusion***

6. Claims 29-30, 32, 36-39, 41-44 are allowed.

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7. Any comments considered necessary by applicant must be submitted no later than the payment of the issue fee and, to avoid processing delays, should preferably accompany the issue fee. Such submissions should be clearly labeled "Comments on Statement of Reasons for Allowance."

8. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Delia M. Ramirez, Ph.D., whose telephone number is (571) 272-0938. The examiner can normally be reached on Monday-Friday from 9:30 AM to 6:00 PM. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Robert B. Mondesi, can be reached at (571) 272-0956. Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is (571) 272-1600.

/Delia M. Ramirez/

Primary Patent Examiner  
Art Unit 1652

DR  
August 6, 2010